

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>16356/PCT ge</b>	FOR FURTHER ACTION	See Form PCT/IPEA/416																								
International application No. <b>PCT/EP2004/006799</b>	International filing date (day/month/year) <b>23.06.2004</b>	Priority date (day/month/year) <b>23.06.2003</b>																								
International Patent Classification (IPC) or national classification and IPC																										
Applicant <b>FRAUNHOFER-GESELLSCHAFT ZUR FÖRDERUNG DER ANGEWANDTEN FORSCHUNG E. V.</b>																										
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>5</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <table border="0"><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>			<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report																									
Name and mailing address of the IPEA/EP	Authorized officer																									
Facsimile No.	Telephone No.																									

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/EP2004/006799

Box No. I	Basis of the report
1.	<p>With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:</p> <p><input type="checkbox"/> international search (Rule 12.3 and 23.1(b))</p> <p><input type="checkbox"/> publication of the international application (Rule 12.4)</p> <p><input type="checkbox"/> international preliminary examination (Rule 55.2 and/or 55.3)</p>
2.	<p>With regard to the elements of the international application, this report is based on <i>(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)</i>:</p> <p><input type="checkbox"/> the international application as originally filed/furnished</p> <p><input checked="" type="checkbox"/> the description:</p> <p>pages <u>1-26</u> _____ as originally filed/furnished</p> <p>pages* _____ received by this Authority on _____</p> <p>pages* _____ received by this Authority on _____</p> <p><input checked="" type="checkbox"/> the claims:</p> <p>nos. _____ as originally filed/furnished</p> <p>nos.* _____ as amended (together with any statement) under Article 19</p> <p>nos.* <u>1-33</u> _____ received by this Authority on <u>20.04.2005 with letter</u></p> <p>nos.* _____ received by this Authority on <u>of 20.04.2005</u></p> <p><input checked="" type="checkbox"/> the drawings:</p> <p>sheets <u>1/3-3/3</u> _____ as originally filed/furnished</p> <p>sheets* _____ received by this Authority on _____</p> <p>sheets* _____ received by this Authority on _____</p> <p><input type="checkbox"/> a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.</p>
3.	<p><input type="checkbox"/> The amendments have resulted in the cancellation of:</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (<i>specify</i>): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (<i>specify</i>): _____</p>
4.	<p><input type="checkbox"/> This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).</p> <p><input type="checkbox"/> the description, pages _____</p> <p><input type="checkbox"/> the claims, nos. _____</p> <p><input type="checkbox"/> the drawings, sheets/figs _____</p> <p><input type="checkbox"/> the sequence listing (<i>specify</i>): _____</p> <p><input type="checkbox"/> any table(s) related to sequence listing (<i>specify</i>): _____</p>

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 29-31 with regard to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 29-31 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 29-31 relate to subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, no expert opinion has been established in respect of the industrial applicability of the subject matter of said claims (PCT Article 34(4)(a)(i)).

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for said claims Nos. \_\_\_\_\_

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-21	YES
	Claims	22-33	NO
Inventive step (IS)	Claims	1-21	YES
	Claims	22-33	NO
Industrial applicability (IA)	Claims	1-28, 32, 33	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
1. Reference is made to the following documents:			
D1: WO 00/78929 A (BONNER WEIR SUSAN; TANEJA MONICA (US); JOSLIN DIABETES CT INC (US)) 28 December 2000 (2000-12-28)			
D2: BONNER-WEIR ET AL: "In vitro cultivation of human islets from expanded ductal tissue" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, Vol. 97, No. 14, 5 July 2000 (2000-07-05), pages 7999-8004, XP002144480 ISSN: 0027-8424			
D3: WO 02/059278 A (KIM JONG-HOON; US GOVERNMENT (US); BLONDEL OLIVER (US); MC KAY RONALD) 1 August 2002 (2002-08-01)			
D4: WO 02/086107 A (INST PFLANZENGENETIK & KULTUR; ST-ONGE LUC (DE); HOFFMANN URSULA (DE)) 31 October 2002 (2002-10-31)			
D5: RAMIYA VIJAYAKUMAR K ET AL: "Reversal of insulin-dependent diabetes using islets generated in vitro from pancreatic stem cells" NATURE MEDICINE, Vol. 6, No. 3, March 2000, pages 278-282, XP000864764			

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
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2. **Novelty and inventive step** (PCT Article 33(2) and (3))

The present application discloses a method for differentiating pluripotent stem cells in cells that produce a pancreatic hormone (i.e. insulin). The method is based on the observation that adult pluripotent stem cells can be isolated and cultivated from exocrine glandular tissue. Under culture conditions which permit three-dimensional contact of the cells (e.g. in suspended droplets), three-dimensional cell aggregates with a tissue-like structure, the organoid bodies, spontaneously develop from such stem cells. The cells then differentiate in the organoid bodies into hormone-producing cells.

**D1** and **D2** indicate that exocrine cells from the pancreas can dedifferentiate into pluripotent stem cells. Said stem cells can then redifferentiate into insulin-secreting cells and form Langerhans' islands. **D1** and **D2** do not, however, indicate that the cells have the capacity to form organoid bodies. **D1** and **D2** therefore do not anticipate the novelty and inventive step in the new claims 1-21. Since, however, the cells and compositions as per claims 22-33 are characterised only by the method by means of which they can be obtained ("product-by-process" claims), **D1** and **D2** anticipate the novelty and inventive step in claims 22-33 (PCT Article 33(2) and (3)).

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**D3** and **D4** disclose the differentiation of embryonic stem cells to endocrine cells, e.g. insulin-secreting cells. Under certain culture conditions, embryonic stem cells form embryoid bodies, from which endocrine precursor cells are selected, which subsequently differentiate into endocrine cells. Artificial Langerhans' islands are explicitly disclosed in **D3**. It follows that **D3** and **D4** deprive the subject matter of claims 22-33 of novelty and inventive step (PCT Article 33(2) and (3)).

For the sake of completeness it is mentioned that **D5** discloses structures in the adult pancreas which contain stem cells (islet-producing stem cells, iPSCs). Said stem cells can differentiate into Langerhans' islands. **D5** therefore also deprives claims 22-33 of novelty and inventive step.

3. **Industrial applicability** (PCT Article 33(4))

The claims for which an expert opinion can be established (see Box III) meet the requirements of PCT Article 33(4).

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

**Box I****Basis of the report**

1. The amendments submitted with the letter of 20 April 2005 are formally acceptable, since they do not go beyond the disclosure in the originally filed application.